REMARKS

Claims 1-12 and 16-37 are pending. Claims 16-37 are withdrawn. Claims 13-15 and 28-49 are cancelled.

Applicants have reached out to the Examiner to schedule an interview. Applicants respectfully request that the Examiner grant Applicant's request for an interview prior to the mailing of any further action on the merits.

Rejections under 35 U.S.C. § 103(a)

Claims 1-12 are rejected under 35 U.S.C. § 103(a) over Tsien et al., US Patent No. 6,469,154 ("Tsien") and McWherter et al., 38:4564-4571, 1999 ("McWherter"). Applicants respectfully disagree and traverse the rejection.

Claims 1, 4, 7, and 10, from which the remaining claims depend, are directed to methods for assembling a modulatable fusion molecule polypeptide. In support of the obviousness rejection, the Examiner points to Tsien et al., column 2, first full paragraph. Regarding Tsien, the Examiner states, "However, in Tsien et al., . . . the insertion of a sensor polypeptide into the output-generating protein causes the output to change (modulate) when the sensor is bound (input) (Action, page 2, last paragraph)." The claimed invention differs from the invention of Tsien, at least in part, because the only signal described by Tsien is a **fluorescent signal**. For example, at column 2, first full paragraph, Tsien states:

> The inventors have discovered that when a sensor polypeptide is inserted into an Aequorea-related fluorescent protein (e.g., Green Fluoresent Protein (GFP), Yellow Florescent Protein (YFP), or Cyan Fluoresent Protein (CFP) to form a construct, interaction of the sensor polypeptide with a biological, chemical, electrical or physiological parameter, for example, results in **a change in fluorescence** of the florescent protein.

In contrast, Applicants' claims are directed to a modulatable fusion polypeptide having the output signal functionally coupled to the input signal **where the output signal is not fluorescence**. Tsien

fails to envision the modulation of any signal other than a fluoresent signal. Thus, Tsien fails to teach or suggest Applicants' claimed invention.

The Examiner cites McWherter to remedy the deficiencies of Tsien. However, this reliance is unavailing because the molecules described in McWherter are **not** modulatable fusion proteins because the output signal of one ligand is **not** influenced by the input signal of the other ligand. McWherter describes an IL-3R agonist domain fused to a cpG-CSF domain. In the fusion protein described by McWherter the insertion of the first agonist stabilizes the structure of the second agonist. This stabilization is **not** dependant on **any input signal**, it is merely a constitutive aspect of the structure of the fusion protein. Accordingly, the fusion protein described by McWherter is not a modulatable fusion protein, and McWherter fails to remedy the deficiency of Tsien.

CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance. If a telephone conversation with Applicants' agent would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned agent at (617) 517-5580.

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Respectfully submitted,
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